

CORRECTED VERSION

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31/496, 31/506, 31/5377, 31/541, 31/551, C07D 471/04,
401/14, 405/14, A61P 37/02

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(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
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SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a
patent (Rule 4.17(ii))
- as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii))

Published:

- with international search report

(88) Date of publication of the international search report:
30 June 2005

(48) Date of publication of this corrected version:
18 May 2006

(15) Information about Correction:
see PCT Gazette No. 20/2006 of 18 May 2006

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **ALKOXY SUBSTITUTED IMIDAZOQUINOLINES**

(57) Abstract: Imidazoquinoline compounds with an alkoxy substituent at the 6, 7, 8, or 9-position, pharmaceutical compositions containing the compounds, intermediates, methods of making, and methods of use of these compounds as immunomodulators, for inducing or inhibiting cytokine biosynthesis in animals and in the treatment of diseases including viral, and neoplastic, are disclosed.

WO 2005/032484 A3

63. The compound or salt of claim 55 or claim 62 wherein R_6 is =O or =S, a and b are each independently 1 to 3, and A' is selected from the group consisting of $-CH_2-$, $-S(O)_2-$, and $-O-$.

5

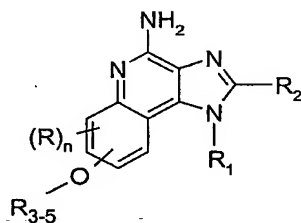
64. The compound or salt of claim 55, claim 62, or claim 63 wherein Z_a is methylene, R_6 is =O, a is 1 or 2, b is 2, and A' is $-CH_2-$.

10

65. The compound or salt of claim 55, claim 62, or claim 63 wherein Z_a is methylene, R_6 is =O, a and b are each 2, and A' is $-O-$.

66. The compound or salt of claim 55 wherein Z_a is a bond or alkylene.

67. A compound of the formula (VII):



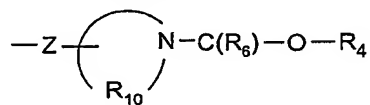
15

VII

wherein:

R_{3-5} is selected from the group consisting of

$-Z-N(R_8)-C(R_6)-O-R_4$,



20

, and

$-Z-N(R_8)-C(R_6)-C(R_6)-R_4$;

Z is selected from the group consisting of alkylene, alkenylene, and alkynylene, wherein alkylene, alkenylene, and alkynylene can be optionally interrupted with one or more $-O-$ groups;

25

R is selected from the group consisting of alkyl, alkoxy, hydroxy, halogen, and trifluoromethyl;

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 58915WO006	FOR FURTHER ACTION	See item 4 below
International application No. PCT/US2004/032616	International filing date (<i>day/month/year</i>) 01 October 2004 (01.10.2004)	Priority date (<i>day/month/year</i>) 03 October 2003 (03.10.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant 3M INNOVATIVE PROPERTIES COMPANY		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 7 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 15%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 35%;">Box No. I</td> <td style="width: 50%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VII	Certain defects in the international application																							
<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 740 14 35	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 2px;">Date of issuance of this report 03 April 2006 (03.04.2006)</td> </tr> <tr> <td style="padding: 2px;">Authorized officer Athina Nickitas-Etienne</td> </tr> <tr> <td style="padding: 2px;">Telephone No. +41 22 338 89 95</td> </tr> </table>	Date of issuance of this report 03 April 2006 (03.04.2006)	Authorized officer Athina Nickitas-Etienne	Telephone No. +41 22 338 89 95
Date of issuance of this report 03 April 2006 (03.04.2006)				
Authorized officer Athina Nickitas-Etienne				
Telephone No. +41 22 338 89 95				

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
DEAN A. ERSFELD
OFFICE OF INTELLECTUAL PROPERTY COUNSEL
POST OFFICE BOX 33427
SAINT PAUL, MN 55133-3427

PCT

REC'D 20 APR 2005

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year) **18 APR 2005**

FOR FURTHER ACTION

See paragraph 2 below

Applicant's or agent's file reference

58915WO006

International application No.

PCT/US04/32616

International filing date (day/month/year)

01 October 2004 (01.10.2004)

Priority date (day/month/year)

03 October 2003 (03.10.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/4745, 31/496, 31/506, 31/5377, 31/541, 31/551; C07D 471/04, 401/14, 405/14; A61P 37/02 and US Cl.: 514/293, 232.8, 253.03, 218, 214.03, 217.07, 273, 228.5; 546/82; 544/126, 60, 361; 540/575, 585, 597

Applicant

3M INOVATIVE PROPERTIES COMPANY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

Evelyn Huang

Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/32616

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☐ in written format
☐ in computer readable form

c. time of filing/furnishing

- ☐ contained in international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/32616

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
- ☒ claims Nos. 5-10, 14, 21, 25, 34, 38, 41, 64, 65 and 76-90

because:

- ☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 5-10, 14, 21, 25, 34, 38, 41, 64, 65 and 76-90 are so unclear that no meaningful opinion could be formed (*specify*):

They are improperly multiply dependent claims. PCT Rule 6.4 (a).

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for said claims Nos. _____
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | | |
|----------------------------|--------------------------|-----------------------------------|
| the written form | <input type="checkbox"/> | has not been furnished |
| | <input type="checkbox"/> | does not comply with the standard |
| the computer readable form | <input type="checkbox"/> | has not been furnished |
| | <input type="checkbox"/> | does not comply with the standard |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/32616

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☒ paid additional fees
 - ☐ paid additional fees under protest
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:

- ☒ all parts.
- ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/32616

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

Inventive step (IS)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

Industrial applicability (IA)

Claims Please See Continuation Sheet YES

Claims Please See Continuation Sheet NO

2. Citations and explanations:

Claims 1-4, 11-13, 15-20, 22-24, 26-33, 35-37, 39, 40, 42-63, and 66-75 meet the criteria set out in PCT Article 33(2)-(3), because the closest prior art, US 6,200,592 B1, only teaches alkoxy, and does not teach or fairly suggest the instant -O-R₃ substituent on the imidazoquinoline.

Claims 91-93 meet the criteria set out in PCT Article 33(2)-(3), because the closest prior art, US 4,698,348 A, only teaches methoxy, and does not teach or fairly suggest the instant -O-R₃ substituent on the imidazoquinoline.

Claims 1-4, 11-13, 15-20, 22-24, 26-33, 35-37, 39, 40, 42-63, 66-75, and 91-93 meet the criteria set out in PCT Article 33(4), and thus find industrial applicability because the subject matter claimed can be made or used in the pharmaceutical industry as immunomodulating agent in treatment of diseases.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/32616

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V.1. Reasoned Statements:

The opinion as to Novelty was positive (Yes) with respect to claims 1-4, 11-13, 15-20, 22-24, 26-33, 35-37, 39, 40, 42-63, 66-75, 91-93

The opinion as to Novelty was negative (No) with respect to claims NONE

The opinion as to Inventive Step was positive (Yes) with respect to claims 1-4, 11-13, 15-20, 22-24, 26-33, 35-37, 39-40, 42-63, 66-75, 91-93

The opinion as to Inventive Step was negative (NO) with respect to claims NONE

The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-4, 11-13, 15-20, 22-24, 26-33, 35-37, 39, 40, 42-63, 66-75, 91-93

The opinion as to Industrial Applicability was negative (NO) with respect to claims NONE